UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/373,403	08/12/1999	WILLIAM R. ARATHOON	P1099C1	2534

23552 7590 05/04/2005

MERCHANT & GOULD PC
P.O. BOX 2903
MINNEAPOLIS, MN 55402-0903

EXAMINER	
HOLLERAN, ANNE L	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 05/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/373,403	ARATHOON ET AL.	
	Examiner	Art Unit	
	Anne Holleran	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 February 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-43 and 45-55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-43 and 45-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed February 4, 2005 is acknowledged. Claim 44 was canceled. Claims 30-43 and 45-55 are pending and examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections/Objections Withdrawn:

3. The rejection of claims 41-55 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the amendment.

4. The rejection of claims 41 and 42 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for isolated host cells comprising nucleic acids encoding the multispecific antibody of claim 30, does not reasonably provide enablement for host cells comprised within a transgenic animal or an animal or human being having been treated by gene therapy is withdrawn in view of the amendment of "host cells" to "isolated host cells".

Claim Rejections/Objections Maintained:

5. The provisional rejection of claims 30-43 and 45-49 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 30-51 of copending

Application No. 09/863,693 is maintained for the reasons of record. Applicants have indicated that upon an indication of allowable subject matter, a terminal disclaimer may be filed if appropriate.

6. The provisional rejection of claims 30-43 and 45-49 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 47-63 of copending Application No. 09/520,130 is maintained for the reasons of record. Applicants have indicated that upon an indication of allowable subject matter, a terminal disclaimer may be filed if appropriate.

7. The provisional rejection of claims 30-43 and 45-49 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-29 of copending Application No. 10/143,437 is maintained for the reasons of record. Applicants have indicated that upon an indication of allowable subject matter, a terminal disclaimer may be filed if appropriate.

8. Claims 30-42 remain rejected under 35 U.S.C. 112, first paragraph, on the grounds that the applicants were not in possession of the claimed inventions at the time of filing, because the disclosure of the specification fails to adequately describe the claimed genus of compounds to be made in the claimed methods and encoded by the nucleic acids of the claimed host cells is maintained for the reasons of record. This is a new matter rejection.

Applicants' arguments have been carefully considered but fail to persuade. Applicants point to page 97, line 28 – page 98, line 3 as support for the concept of multispecific antibodies comprising more than one light chain, where the light chains have at least 98% sequence identity and only differ from one another at amino acid positions outside of the CDR regions. The passage pointed to appears to be a discussion concerning whether one may substitute one light chain for another in a specific scFv ("Alternatively, according to the invention, such light chains having 98-99% sequence identity with the light chian of a prospective paired scFv (Axl.78, for example) may be substituted with the paired light chain and retain binding specificity"). This sentence does not appear to be support for the concept of multispecific antibodies having more than one light chain, but instead appears to be support for making alternative versions of specific scFv molecules. Therefore, the rejection is maintained for the reasons of record.

The original rejection is reiterated below:

The basis for this rejection is that the amendment to the specification to recite claims drawn to methods of making multispecific antibodies comprising binding domains, where the binding domains are made up of a heavy and light chain, and where the light chain is not the same for all of the binding domains is not supported by the specification. Therefore, the recitation of claim 30 "where the light chains of the first and additional polypeptides each have three CDR regions, and have at least 98% sequence identity and only differ from one another at amino acid positions outside of the CDR regions" is not supported by the specification as originally filed. The specification teaches methods of making multispecific antibodies, where the each of the binding domains comprises a "common light chain". The specification defines

"common light chain" or "common amino acid sequence of the light chain" on page 21, and as an amino acid sequence of ***the*** light chain in the multispecific antibody. There does not appear to be any contemplation of multispecific antibodies comprising more than one light chain (i.e., there appears to be only the contemplation that the same light chain is used for all of the binding domains present in the multispecific antibody). Even a difference of 1 amino acid between the two light chains results in a bispecific antibody having two different light chains, and there is no support in the specification that demonstrates that applicant conceived of a method of making multispecific antibodies having two different light chains. Other instances in the specification that indicate that applicant conceived of methods of making bispecific antibodies where all of the binding domains comprise a light chain having the same sequence is found at page 10, lines 20-21; page 10, line 29 – page 11, line 1; page 12, line 15-line 24; page 13, lines 6-13; page 16, line 1-15; page 56, lines 13-29; page 95, lines 25-28; and page 103, lines 5-8.

Applicants have pointed to passages (page 97-98) in the specification and assert that these passages provide support for the concept of multispecific antibodies comprising light chains where the light chains have at least 98% sequence identity to each other and only differ from one another at amino acid positions outside the CDR regions. However, this teaching of the specification appears to be directed to the process of selecting a light chain that will be used in the process of making a multispecific antibody (i.e. selecting a common light chain). The teachings on page 97 of the specification do not provide support for bispecific antibodies having two different light chains, but instead are directed to a process for identifying one light chain that may be useful in making a bispecific antibody. Applicants are reminded that the description requirement is severable from the enablement requirement.

9. Claims 50 and 53-55 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for the reasons of record. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Applicants' arguments have been carefully considered but fail to persuade. Applicants assert that the specification explicitly teaches that a light chain having at least 98% identity to a second light chain can be substituted with that light chain while having little or no effect on antigen binding. Applicants failed to support this assertion by pointing to a passage in the specification, and as discussed in the previous Office action, the passages originally pointed to by applicant for support for these new claims teach light chains with differences occurring outside the CDRs. Therefore, a claim that recites the phrase at least 98% sequence identity without qualifying the phrase that the differences are out the CDRs contains new matter because the concept of "at least 98% sequence identity" is broader than the concept presented in the specification of "at least 98% sequence identity, where the differences occur outside the CDRs". Therefore, the rejection is maintained.

The original rejection is reiterated below:

The basis for this rejection is that the addition of claims 50 and 53-55, which are drawn to methods of making multispecific antibodies where the first and additional polypeptides each comprise a binding domain, the binding domains comprising a heavy chain and a common light chain, where the common light chain of the first and additional polypeptides has at least 98% sequence identity to each light chain of a first antibody and at least one additional antibody is not

supported in the specification. The passages pointed to by applicant include the finding that the differences between the sequences of the compared light chains occurs outside the CDRs. This limitation is not present in the claims and the lack of this limitation is a broadening of scope that was not originally contemplated when the application was filed.

New Grounds of Rejection:

10. Claims 51 and 52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 51 and 52 are indefinite because the phrase "the common light chains", which is plural, lacks antecedent basis in claim 50, which refers to "the common light chain of the first and additional polypeptides", which appears to be singular.

11. Claim 52 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 52 appears to broaden the scope of claim 51, or 50, from which claim 52 ultimately depends, because 51 appears to be drawn to a method for making a multispecific antibody with two different light chains instead of one light chain. This interpretation is made because of the claim recites that the common light chains each have at least 3 CDRs, and the common light chains only differ at amino acid positions outside of the

CDRs, whereas claim 50 appears to have one light chain common to all of the binding domains in the multispecific antibody and claim 51 only has one light chain (100% identity).

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the Office should be directed to Anne Holleran, Ph.D. whose telephone number is (571) 272-0833. Examiner Holleran can normally be reached Monday through Friday, 9:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at (571) 272-0787.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (703) 571-1600.

Anne L. Holleran
Patent Examiner
April 29, 2005

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER

05/02/05